

Fig. 1

## SEQ ID NO 1

-496 ACCATAGTCA TCCATATTGA TATTTATAT CATCTCAACT TCTCTTGCC AACTTGACC TACTGTGCA ATTATTTTAC ATTCTCTGG CTCTGTTTTC  
-396 ATTTATATTT AATTCAGAA ACCACATCAA GTCTTTCAG AATGAAGTAG AGCATTAAAGA AGTAGAGATG TACACACGCA TCTCTAAAAT CAGCCATGCC  
-296 TAGGCAAAGC AGCTTGCCT TAAACACCCA ATACATTTT CATGATTGTG TTGAAGTGAA GTAACTAAC CGTTTTTAT ATCCTTCAAA ATAAGGTGGA  
-196 TAGGAATGCT TTCAGCCCTT TTCAATAGCT TTGATTATCT TGTTTTGTG AGATCCCTCC TCTTGGTTTG ATCATAGTAG TTACTGTATT TCTTTTATA  
-96 AGCTGGTCTG CAAAGGGTAG GGCTTGCAGA CCATTCGAAA GTGTGACGG CTGTGAGTCA TATGTCTGAA GGTGGAATC TGAAGCCAGA CTATCTATGT  
+5 GAAGGCACAA GCTGCTGTTA TATACACAG AGTGAAGTGA GCATCAGTCA GAAAAGTCT ATGTTTGCAG AAATACAGAT CCAAGACAAA GACAGG ATG  
rev TATA box

++++++ ++++++  
AP-1 C/EBP +1

+104 GGC ACT GCT GGA AAA GTAAGTGAACATT Intron 1 (5.6 kb) TTGCTATTCTTAG GTT ATT AAA TGC AAA GCA GCT GTG  
G T A G K \*\* \*\* V I K C K A A V  
1 10

CTT TGG GAG CAG AAG CAA CCC TTC TCC ATT GAG GAA ATA GAA GTT GCC CCA CCA AAG ACT AAA GAA GTT CGC ATT AAG GTA  
L W E Q K Q P F S I E E I E V A P P K T K E V R I K \*\*  
20 30

AGCGTGAGCCT Intron 2 (1.0 kb) TGTCTTGAACACAG ATT TTG GCC ACA GGA ATC TGT CGC ACA GAT GAC CAT GTG ATA  
\*\* I L A T G I C R T D D H V I  
40 50

AAA GCA ACA ATG GTG TCC AAG TTT CCA GTG ATT GTG GGA CAT GAG GCA ACT GGG ATT GTA GAG AGC ATT GGA GAA GGA GTG  
K G T M V S K F P V I V G H E A T G I V E S I G E G V  
60 70 80

ACT ACA GTG AAA CCA G GTATATGCAGGTG Intron 3 (0.3 kb) ATTTTTCCTGTAG GT GAC AAA GTC ATC CCT CTC TTT  
T T V K P \*\* \*\* G D K V I P L F  
90

CTG CCA CAA TGT AGA GAA TGC AAT GCT TGT CGC AAC CCA GAT GGC AAC CTT TGC ATT AGG AGC GA GTAGGTTTCAGTCAT  
L P Q C R E C N A C R N P D G N L C I R S D \*\*  
100 110

Intron 4 (0.1 kb) TGATGTATCAACAG T ATT ACT GGT CGT GGA GTA CTG GCT GAT GGC ACC ACC AGA TTT ACA TGC AAG GGC  
\*\* I T G R G V L A D G T T R F T C K G  
117 119 120 130

AAA CCA GTC CAC CAC TTC ATG AAC ACC AGT ACA TTT ACC GAG TAC ACA GTG GTG GAT GAA TCT TCT GTT GCT AAG ATT GAT  
K P V H H F M N T S T F T E Y T V V D E S S V A K I D  
140 150 160

GAT GCA GCT CCT CCT GAG AAA GTC TGT TTA ATT GGC TGT GGG TTT TCC ACT GGA TAT GGC GCT GCT GTT AAA ACT GGC AAG  
D A A P P E K V C L I G C G F S T G Y G A A V K T G K  
170 180

GTAAGAAACAGGTA Intron 5 (7.1 kb) CATTCCTCTCCACAG GTC AAA CCT GGT TCC ACT TGC GTC GTC TTT GGC CTG GGA  
\*\* V K P G S T C V V F G L G  
190 200

GGA GTT GGC CTG TCA GTC ATC ATG GGC TGT AAG TCA GCT GGT GCA TCT AGG ATC ATT GGG ATT GAC CTC AAC AAA GAC AAA  
G V G L S V I H G C K S A G A S R I I G I D L N K D K  
210 220

TTT GAG AAG GCC ATG GCT GTA GGT GCC ACT GAG TGT ATC AGT CCC AAG GAC TCT ACC AAA CCC ATC AGT GAG GTG CTG TCA  
F E K A M A V G A T E C I S P K D S T K P I S E V L S  
230 240 250

GAA ATG ACA GGC AAC AAC GTG GGA TAC ACC TTT GAA GTT ATT GGG CAT CTT GAA ACC ATG GTAAGACCCAAAAT Intron 6  
E M T G N N V G Y T F E V I G H L E T H \*\*  
260 270

(1.4 kb) CCGTTTTAACTCAG ATT GAT GCC CTG GCA TCC TGC CAC ATG AAC TAT GGG ACC AGC GTG GTT GTA GGA GTT CCT  
\*\* I D A L A S C H M N Y G T S V V V G V P  
280 290

CCA TCA GCC AAG ATG CTC ACC TAT GAC CGG ATG TTG CTC TTC ACT GGA CGC ACA TGG AAG GGA TGT GTC TTT GGA G GTCAG  
P S A K M L T Y D P M L L F T G R T W K G C V F G \*\*  
300 310 320

GAAAGCAAAG Intron 7 (3.2 kb) TTGCTTATTTCAG GT TTG AAA AGC AGA GAT GAT GTC CCA AAA CTA GTG ACT GAG TTC  
\*\* G L K S R D D V P K L V T E F  
330

CTG GCA AAG AAA TTT GAC CTG GAC CAG TTG ATA ACT CAT GTT TTA CCA TTT AAA AAA ATC AGT GAA GGA TTT GAG CTG CTC  
L A K K F D L D Q L I T H V L P F K K I S E G F E L L  
340 350 360

AAT TCA GGA CAA AG GTAAGTCTTCTTAT Intron 8 (2.3 kb) CATTTTACATTTCAG C ATT GGA ACG GTC CTG ACG TTT TGA  
N S G Q S \*\* \*\* I R T V L T F A  
370 374

GATCCAAAGT GCCAGGAGGT CTGTGTGTC ATGGTGAAGT GGAGTTTCTC TTGTGAGAGT TCCC

Fig. 2

>gi|642473|gb|U16286|HSADHVII1 Human class IV alcohol dehydrogenase (ADH7) gene, exon 1

ACCATAGTCA TCCATATTGA TATTTTATAT CATCTCAACT TCTCTTGCCC AAACCTTGACC TACTGTTGCA ATTATTTTAC ATTCCTTGG  
CTCTGTTTTC ATTTATATTT AATTCCAGAA ACCACATCAA GTCTTTGCAG AATGAAGTAG AGCATTAAAG AGTAGAGATG TACACACGCA  
TCTCTAAAT CAGCCATGCC TAGGCAAAGC AGCTTGCACT TAAACACCCA ATACATTTT CATGATTGTG TTGAAGTGAA GTAACCTAAC  
CCGTTTTTAT ATCCTTCAA ATAAGGTGGA TAGGAATGCT TTCAGCCCTT TCAATAGCT TTGATTATCT TGTTTTTTGT AGATCCCTCC  
TCTTGTTTTG ATCATAGTAG TTAAGTATT TCTTTTATA AGCTGGTCTG CAAAGGGTAG GGCTTGCAGA CCATTGCAAA GTTGTGACGG  
CTGTAGTCA TATTGCTGAA GGTGGAACCT TGAAGCCAGA CTATCTATGT GAAGGCACAA GCTGCTGTTA TATACAACAG AGTGAACCTGA  
GCATCAGTCA GAAAAAGTCT ATGTTTGCAG AAATACAGAT CCAAGACAAA GACAGGATGG GCACTGCTGG AAAAGTAAGT GGAACATTTT  
TGTCCCTCC TCATCATGAC CTAATGATGT GAGGCTGATA CTTAGAACTT TGAATCCATT AAAGTAATTA AACACTTGGA GATATTCCTT  
GAGGAATGAA ATGCTTGGTG AGCAGGCATA CAGTGAGGGA AACACTGGAT ATGGTGTTTC AGAGAATGTC AGTGAAGCA GGGTAAGTT  
GGAAATAGTA TATCCAATGT CAGCAAGACA TTGGTGGAAT ATAGAGAAAT TGATTATAT TGGCATTATT CATAATTTGA TTCCGGATA  
GCTGGGCAAT TGCTCCAGGA AGCCAAATGT TTCCACAAGG AACTTCAAT CGTCTCAGTA GCATGTGCTG CACTCGCTGC  
AG

>gi|642474|gb|U16287|HSADHVII2 Human class IV alcohol dehydrogenase (ADH7) gene, exon 2

TAGGTGACCA TGGATCCATC ATTTAGTCAC TCTGGGCTGC ATGTCTCATG CCTTAAGCAA AGGCACACAC AAGATGATTT ATAAGGCTTA  
TAATACTAGT GTTTGATGAA AATCATTCTG GAAACCTTAA AATATTATAT ATGCTCTTCT GTTCATATTT ATACTAGTCA GGGAGTCTGT  
AAGTTAAAGG CATAATTCAG ACCCAATTATA ATACTTGCTT ATTTCTTAGG TTATTAAATG CAAAGCAGCT GTGCTTTGGG AGCAGAAGCA  
ACCCCTCTCC ATTGAGGAAA TAGAAGTTGC CCCACCAAAG ACTAAAGAAG TTCGCATTAA GGTAAGCGTG AGCCCTAGAG AACTTAAGCC  
AAAAGCGTTA TCAAACTTAT ATTGAATATA GCACGTGTTGT GAGGCTGGAT TCTTAAATAA GGAGATGCTT CCCATGTTTG GAGTATTAAT  
TCCTTTACTG GCTCTTATAT ATTGTTAAGG ATCTGGTTGT ACTCGATGTG AAATTAATGA GTTCATTATC C

>gi|642475|gb|U16288|HSADHVII3 Human class IV alcohol dehydrogenase (ADH7) gene, exon 3

AACAATTATA ATTTCTTCAA GAAGTTAAAT ATTCTCCCAA CAGTGAAATG ATCAGTTTGT TGATTGGTGC AATGTTTTTG TCTTTGAACA  
CAGATTTTGG CCACAGGAAT CTGTGCGACA GATGACCATG TGATAAAAGG AACATGGTG TCCAAGTTTC CAGTGATTGT GGGACATGAG  
GCAACTGGGA TTGTAGAGAG CATTGGAGAA GGAGTGACTA CAGTGAAACC AGGTATATGC AGGTGTCAA CCACAAGTTT GAAATAATTA  
GGCTTTGATT AGCCTATCAA AGGAAATAGC ACACACTAGG AATTATTAGA GGGATCC

>gi|642476|gb|U16289|HSADHVII4 Human class IV alcohol dehydrogenase (ADH7) gene, exons 4-5

CCTCAACCTT TAGAAGGCAA ACTTACGGTG TTTATAAACC TTAGAATATA TTTTAAAG TTTTACCTAT AGTATGGGCT CAATTCACAT  
TTGTTAATTT CATATTTTAA CATTAAATGAA CAGCATCTTA TATCATGATT TTTTCTGT AGGTGACAAA GTCATCCCTC TCTTCTGCC  
ACAAATGTA GAATGCAATG CTGTGCGCAA CCCAGATGGC AACCTTTGCA TTAGGAGCGA GTAGGTTTCA GTCATTTTAA CTTTAAATGA  
TTTACATTTT TCCTATGCTA ATTTTGAAT TGAATTAATT AATACGTGTA TTTGATGTAT CAAACAGTAT TACTGGTCTG GGAGTACTGG  
CTGATGGCAC CACCAGATTT ACATGCAAGG GCAAACCACT CCACCACTT ATGAACACCA GTACATTTAC CGAGTACACA GTGGTGGATG  
AATCTTCTGT TGCTAAGATT GATGATGCAG CTCCTCTGA GAAAGTCTGT TTAATTGGCT GTGGGTTTTT CACTGGATAT GCGCTGCTG  
TTAAACTG CAAGGTAAGA AACAGGGTAG GCTAGT

>gi|642477|gb|U16290|HSADHVII5 Human class IV alcohol dehydrogenase (ADH7) gene, exon 6

GAGTCACTC ATGATTTGTG TTTTAACTG GAGGCCCTT TCAGGTTTCA CTTTTTGACC CTAACACCTA ACATGTTCAA GAACATTCCT  
CTCCACAGGT CAAACCTGGT TCCACTTGGC TCGTCTTGG CCTGGGAGGA GTTGGCCTGT CAGTCATCAT GGGCTGTAAG TCAGTGGTG  
CATCTAGGAT CATTGGGATG GACCTCAACA AAGACAAATT TGAGAAGGCC ATGGCTGTAG GTGCCACTGA GTGTATCAGT CCCAAGGACT  
CTACCAAAACC CATCAGTAG GTGCTGTCAG AAATGACAGG CAACAACGTG GGATACACCT TTGAAGTTAT TGGGCATCTT GAAACCATGG  
TAAGACCCCA AAATTTG

>gi|642478|gb|U16291|HSADHVII6 Human class IV alcohol dehydrogenase (ADH7) gene, exon 7

AACGATCTCC TCCGTTTTAA ACTCAGATTG ATGCCCTGGC ATCCTGCCAC ATGAACATG GGACCAGCGT GGTGTAGGA GTTCCTCCAT  
CAGCCAAAGT GCTCACCTAT GACCCGATGT TGCTCTTAC TGGACGCACA TGGAAAGGAT GTGTCTTTGG AGGTGAGGAA AGCAAAGCCT  
CTGGATGGGG AGTATGGCT TTCACCTGG TGCTTGGCAA GTGGGAGAAG CCTGTTTCTT CAGGCCTTTC TTCCAAGAA GAGTATGAAG  
TGATCT

>gi|642479|gb|U16292|HSADHVII7 Human class IV alcohol dehydrogenase (ADH7) gene, exon 8

AACACAGGGA AAGTCATAGT GCAGGAAAGA GAAGGAATAA ATATAACATA ATAAAAGATA AGGATTATTT AGTAATGTCT AAAGAGAAAA  
TGTGTCTTA TTTGCAGGT TGAAGAGCAG AGATGATGTC CCAAACTAG TGAAGTGTCT CTGGCAAAG AAATTTGACC TGGACCAAGT  
GATAACTCAT GTTTTACCAT TTAATAAAT CAGTGAAGGA TTTGAGCTGC TCAATTCAGG ACAAAGGTAA CTGTTTCTTA TGATGA

>gi|642480|gb|U16293|HSADHVII8 Human class IV alcohol dehydrogenase (ADH7) gene, exon 9, and complete cds

TTAAACTATC CTTTCTTGAA AGATATGAAA ACAAGTCATT AAAAATCTC ATTTTACATT TCAGCATTCG AACGGTCTG ACCTTTTGAG  
ATCCAAAGTG GCAGGAGTCT TGTGTTGTA TGGTGAAGT GAGTTTCTCT TGTGAGAGT CCC

Fig. 3

Fragment number	Size	Contents	Forward and reverse primers
1	450bp	Promoter region, 5' UTR and first exon.	1-F AATCAGCCATGCCTAGGCAAA 1-R GGAGGGGACAGAAATGTTCCA
2	405bp	Second exon and parts of flanking introns	2-F GGCTGCATGTCTCATGCCTT 2-R CCAAACATGGGAAGCATCTCC
3	260bp	Third exon and parts of flanking introns	3-F CAGTTTGTTGATTGGTGCAATGTT 3-R TGTGTGCTATTTCTTTGATAGGCT
4	510bp	Fourth and fifth exon and fourth intron and parts of flanking introns	4-F ATGGGCTCAATTCACATTTGTT 4-R AACTAGCCTACCCTGTTTCTT
5	340bp	Sixth exon and parts of flanking introns	5-F TTCAGGTTTCACTTTTTGACCC 5-R CAAATTTTGGGGTCTTACC
6	260bp	Seventh exon and parts of flanking introns	6-F ATCTCCTCCGTTTTAAACTC 6-R CTCATTCTTGGAAGAAAGGCC
7	265bp	Eighth exon and parts of flanking introns	7-F ACAGGGAAAGTCATAGTGCAGG 7-R TCATCATAAGAAACAGTTAC
8	135bp	Nineth exon and parts of flanking introns	8-F TCCTTTCTTGAAAGATATGAA 8-R CTCCAGTTCACCATGACAACAC

Fig. 4

Name	Fragment no.	Location	Wildtype sequence	Mutated sequence (mutations in bold are underlined)	Restriction enzyme (examples)	Type of mutation
M1	1	promoter	-102 to -88 TTTATAAGTTGGTCT	-102 to -88 TTTATAAG <u>CT</u> GGTCT	Alu I Cvi I	single nucleotide exchange
M2	1	5'-UTR	+20 to +32 TGTTATATACAAC	+20 to +32 TGTTAC <u>AT</u> ACAAC	Mae III	putative TATA-box disrupting
M3	2	second intron	in GDB U16287 nr. 415 to 426 AAATAAGGAGAT	in GDB U16287 nr. 415 to 426 AAATAAG <u>G</u> GGAGAT	-	2bp insertion
M4	3	second intron	in GDB U16288 nr. 81 to 95 TCTTTGAACACAGAT	in GDB U16288 nr. 81 to 95 TCTTTGAG <u>C</u> ACAGAT	BsiHKA I Bsp1286 I	single nucleotide exchange
M5	3	third exon	in GDB U16288 nr. 205 to 218 GGAGAAGGAGTGAC	in GDB U16288 nr. 205 to 218 GGAGAAG <u>C</u> AGTGAC	(TspR I)	amino acid exchange Gly79Ala
M6	4	fourth intron	in GDB U16289 nr. 274 to 287 ACATTTTTCCTATG	in GDB U16289 nr. 274 to 287 ACATTT <u>G</u> TCCTATG	-	single nucleotide exchange
M7	5	sixth exon	in GDB U16290 nr. 180 to 194 GCATCTAGGATCATT	in GDB U16290 nr. 180 to 194 GCATCTAGAATCATT	Hinf I	silent mutation Arg218Arg

Fig. 5

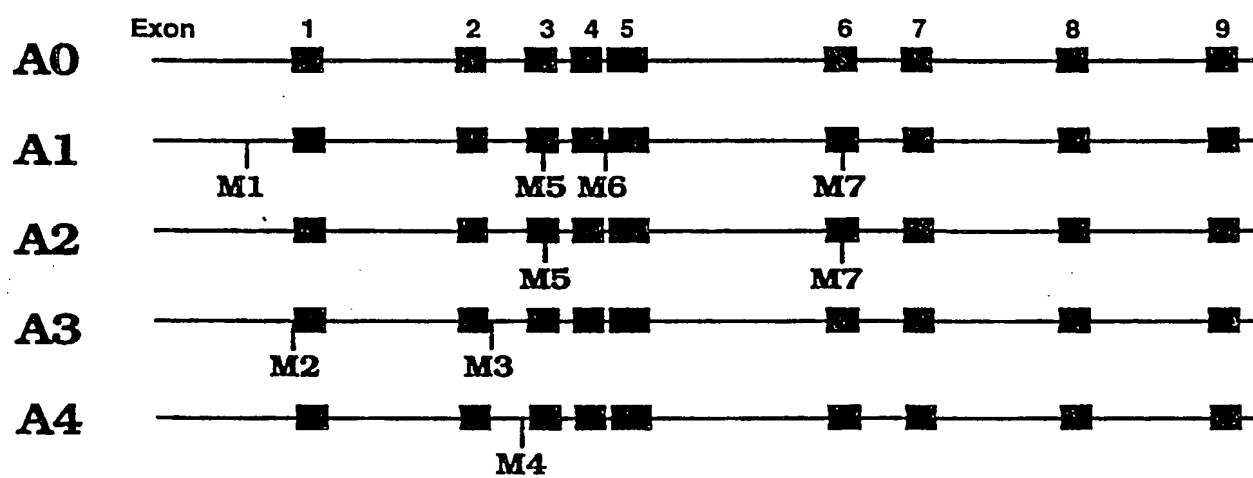


Fig. 6A

	Allele frequency	Number of investigated alleles	Odds ratio	95%CI for the odds ratio	p value
Controls	4.62%	260	-	-	-
Non-familial cases	10.23%	88	2.354	0.9565 to 5.796	0.07
Familial cases	28.57%	28	8.267	3.028 to 22.565	0.0002
Patients total	14.66%	116	3.549	1.635 to 7.703	0.0014

Fig. 6B

Allele number	Allele frequency in controls (n=260)	Number of homozygotes in controls (n=130)	Number of homozygotes in PD patients (n=58)	P
A1	4.62%	0	2	<0.01
A3	11.15%	0	3	<0.05